example, see the notice published in the FEDERAL REGISTER of January 23, 1968 (33 FR 818), regarding rutin, quercetin, et al.

(c) Any marketed drug is a ''new drug'' if any labeling change made after October 9, 1962, recommends or suggests new conditions of use under which the drug is not generally recognized as safe and effective by qualified experts. Undisclosed or unreported side effects as well as the emergence of new knowledge presenting questions with respect to the safety or effectiveness of a drug may result in its becoming a ''new drug'' even though it was previously considered ''not a new drug.'' Any previously given informal advice that an article is ''not a new drug'' does not apply to such an article if it has been changed in formulation, manufacture control, or labeling in a way that may significantly affect the safety of the drug.

(d) For these reasons, all opinions previously given by the Food and Drug Administration to the effect that an article is ''not a new drug'' or is ''no longer a new drug'' are hereby revoked. This does not mean that all articles that were the subjects of such prior opinions will be regarded as new drugs. The prior opinions will be replaced by opinions of the Food and Drug Administration that are qualified and current on when an article is ''not a new drug,'' as set forth in this subchapter.

[39 FR 11680, Mar. 29, 1974]

§ 310.101 FD&C Red No. 4; procedure for discontinuing use in new drugs for ingestion; statement of policy.

(a) Section 81.10(d) of this chapter published December 11, 1964 (29 FR 16983), terminated the provisional listing of FD&C Red No. 4 for use in drugs that may be ingested and canceled the effectiveness of certificates for this color additive and mixtures containing it as of June 9, 1965 (§ 81.30(c) of this chapter), insofar as ingested drugs are concerned. On August 19, 1965 (30 FR 10289), FD&C Red No. 4 was restored to provisional listing by amendment to § 81.1(a) of this chapter, which restricted the use of color to the terms of § 81.25 of this chapter. The use of FD&C Red No. 4 or mixtures containing it in the manufacture of ingested drugs (except for limited use as provided in § 81.25 of this chapter) will result in adulteration and may constitute grounds for withdrawing approval of drugs for which a new drug approval is in effect.

(b) An approved supplemental new drug application will not be required to provide for discontinuing the use of FD&C Red No. 4 in the manufacture of articles that are the subject of approved new drug applications, provided that the applicant submits to the Food and Drug Administration a written notice of the date on which the change in formulation will be put into effect.

(c) It will be the policy of the Food and Drug Administration to take no action against a drug or applicant where a permitted color additive is substituted for FD&C Red No. 4 in the manufacture of a drug prior to receipt of a written notice of approval of a supplemental new drug application, provided that the applicant submits a satisfactory supplemental application meeting all the following conditions:

(1) The applicant submits a full list of the components and a full statement of the composition of the drug.

(2) The date when the composition of the drug will be changed is stated.

(3) The applicant submits data showing that the change in composition does not interfere with any assay or other control procedures used in manufacturing the drug, or that the assay and other control procedures are revised to make them adequate.

(4) The data available to establish the stability of the revised formulation are included, and if the data are too limited to support a conclusion that the drug will retain its declared potency for a reasonable marketing period, a commitment from the applicant:

(i) To test the stability of marketed batches at reasonable intervals;

(ii) To submit the data as they become available; and

(iii) To recall from the market any batch found to fall below the approved specifications for the drug.

(d) When a supplemental application proposes the change prescribed in paragraph (c) of this section and the applicant informs the Food and Drug Administration that the changes have

been put into effect, such notification will be regarded as an agreement by the applicant to an extension of the time for formal action on the supplemental application.

(e) Except as provided in paragraph (c) of this section, no provision of this statement of policy shall limit the authority of the Secretary of Health and Human Services or of the Commissioner of Food and Drugs to suspend or withdraw approval of a new-drug application as prescribed by section 505(e) of the act or to initiate any other regulatory proceedings with respect to a drug or applicant under the provisions of the act.

[39 FR 11680, Mar. 29, 1974, as amended at 42 FR 15674, Mar. 22, 1977]

§ 310.103 New drug substances intended for hypersensitivity testing.

(a) The Food and Drug Administration is aware of the need in the practice of medicine for the ingredients of a new drug to be available for tests of hypersensitivity to such ingredients and therefore will not object to the shipment of a new drug substance, as defined in § 310.3(g), for such purpose if all of the following conditions are met:

(1) The shipment is made as a result of a specific request made to the manufacturer or distributor by a practitioner licensed by law to administer such drugs, and the use of such drugs for patch testing is not promoted by the manufacturer or distributor.

(2) The new drug substance requested is an ingredient in a marketed new drug and is not one that is an ingredient solely in a new drug that is legally available only under the investigational drug provisions of this part.

(3) The label bears the following prominently placed statements in lieu of adequate directions for use and in addition to complying with the other labeling provisions of the act:

(i) ''Caution: Federal law prohibits dispensing without a prescription''; and

(ii) ''For use only in patch testing''.

(4) The quantity shipped is limited to an amount reasonable for the purpose of patch testing in the normal course of the practice of medicine and is used solely for such patch testing.

(5) The new drug substance is manufactured by the same procedures and meets the same specifications as the component used in the finished dosage form.

(6) The manufacturer or distributor maintains records of all shipments for this purpose for a period of 2 years after shipment and will make them available to the Food and Drug Administration on request.

(b) When the requested new drug substance is intended for investigational use in humans or the substance is legally available only under the investigational drug provisions of part 312 of this chapter, the submission of an ''Investigational New Drug Application'' (IND) is required. The Food and Drug Administration will offer assistance to any practitioner wishing to submit an Investigational New Drug Application.

(c) This section does not apply to drugs or their components that are subject to the licensing requirements of the Public Health Service Act of 1944, as amended. (See subchapter F—Biologics, of this chapter.)

[39 FR 11680, Mar. 29, 1974, as amended at 55 FR 11578, Mar. 29, 1990]

Subpart C—New Drugs Exempted From Prescription-Dispensing Requirements

§ 310.200 Prescription-exemption procedure.

(a) *Duration of prescription requirement.* Any drug limited to prescription use under section 503(b)(1)(C) of the act remains so limited until it is exempted as provided in paragraph (b) or (e) of this section.

(b) *Prescription-exemption procedure for drugs limited by a new drug application.* Any drug limited to prescription use under section 503(b)(1)(C) of the act shall be exempted from prescription-dispensing requirements when the Commissioner finds such requirements are not necessary for the protection of the public health by reason of the drug's toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, and he finds that the drug is safe and effective for use in self-medication as directed in proposed labeling. A proposal to exempt a drug